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Atrophic Gastritis Concurrent with *Helicobacter* Infection in Two Dogs

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Abstract : Two dogs (Case 1: Poodle, 4 years old, spayed female; Case 2: Bulldog, 3 years old, intact female) were referred to us for treatment of vomiting; Case 1 had a history of acute vomiting that started 1 day prior to presentation, and Case 2 had a history of chronic vomiting that started 2 years prior to presentation. The vomiting did not respond to medication in the local animal hospital. Results from abdominal ultrasound examinations showed that case 1 had gastric wall thickening, and case 2 had no remarkable findings. For both cases, we performed gastrointestinal endoscopic examinations, and several biopsy samples were obtained from different gastric areas. On the basis of the results of histopathological examinations, both dogs were diagnosed with atrophic gastritis concurrent with a *Helicobacter* infection. Clinical signs improved after antibiotic therapy. This case report describes the clinical, endoscopic, and histopathological findings of atrophic gastritis concurrent with a *Helicobacter* infection.

Key words **:** atrophic gastritis (AG), dog, endoscopy, *Helicobacter.*

Introduction

Gastritis in dogs is often of undetermined etiology (10). Atrophic gastritis (AG) in dogs is thought to be caused by the cellular infiltration in chronic gastric inflammatory disease or immune responses (6,7,10,12). The severity of the cellular infiltrate is diverse and may lead to mucosal atrophy or fibrosis (7,10).

In human medicine, gastric atrophy is associated with *Helicobacter species (spp.)*, which is an important pathogen and cause of inflammation, and an immune-mediated response (6, 10). Unlike in humans, *Helicobacter* were considered part of the natural gastric flora of dogs because these bacteria are frequently found in healthy dogs, as well as dogs with gastrointestinal symptoms (2,3). However, AG in dogs is infrequently reported and there is a lack of information about the similarities with human *Helicobacter* infections (12).

Case

Case 1 (4-year-old spayed female poodle dog; 5.2 kg) was referred to us with a 2-day history of acute vomiting with severe bloody diarrhea, which had developed one day before presentation. The patient was fed commercial dry food without table foods.

The patient had no remarkable findings on physical examination. The results of a complete blood count (CBC) and serum biochemical profile were within reference ranges. Negative result was obtained from a canine pancreatic lipase immunoreactivity (c-PLI) ELISA (Canine SNAP cPL, IDEXX Laboratories, USA) test. *Parvovirus* (Canine Parvovirus Ag test, Rapigen-inc, Korea) and *Giardia* (Canine Giardia Antigen Test, IDEXX Laboratories, USA) ELISA results were also negative.

Abdominal radiography showed microhepatica and splenomegaly. An abdominal ultrasonography revealed a prominent gastric wall and cholecystitis; therefore, we decided to perform upper and lower gastrointestinal tract endoscopic examinations and biopsies.

Gross endoscopic findings in the stomach (Fig 1A, B) and duodenum (Fig 1C) were not significant, but erythema of the colonic mucosa (Fig 1D, E, F) was observed. Endoscopic biopsy samples from the gastric, duodenal, and colonic mucosa were obtained.

Findings from the histopathological examination confirmed atrophic gastritis concurrent with *Helicobacter* infection and enteritis. The gastric glands were generally atrophic (Fig 3A) and mucus at the mucous layer was significantly increased. Large numbers of *Helicobacter spp*. were detected in the mucus layer and lumen of the gastric glands (Fig 3B). Neutrophilic infiltration of the lamina propria, causing inflammatory reactions of colonic area, was also found. Furthermore, partial crypts were lost and replaced with fibrosis, which may have been due to the neutrophilic enteritis combined with gastritis caused by the *Helicobacter spp.* infection.

We prescribed prednisolone (Solondo, Yuhan Pharma, Korea; 0.5 mg/kg, per oral [PO], twice a day [q 12 h]) and

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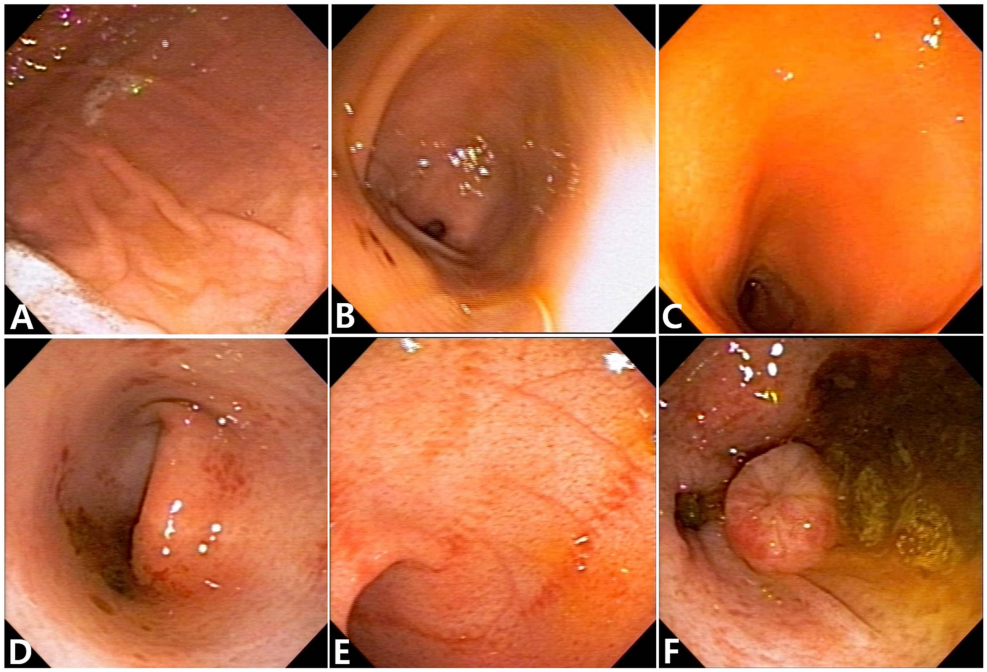

Fig 1. Gastroscopy and colonoscopy of case 1. Gross endoscopic findings in the stomach (A and B) and duodenum (C) were not significant. Patchy erythema of the mucosa was visualized in the colon (D, E, and F).

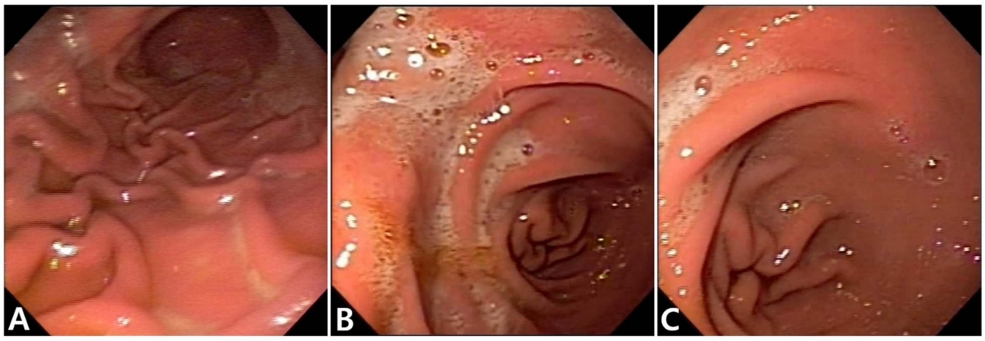

Fig 2. Gastroscopy of case 2. Mild generalized gastric mucosal hyperemia (A, B, and C) and foamy white fluid was visualized (B and C).

ranitidine (Ranis, CMG Pharma, Korea; 2 mg/kg, PO, q 12 h) for the enteritis and amoxicillin-clavulanic acid (Clavamox, Aurobindo Pharma Limited, India; 12.5 mg/kg, PO, q 12 h) and metronidazole (Flasinyl, CJ Cheiljedang Parma, Korea; 10 mg/kg, PO, q 12 h) for the *Helicobacter* infection. The patient's clinical signs gradually improved and subsequently resolved. The prednisolone taper was started at 12 days after initiating treatment depending on the resolution of diarrhea. All medication was discontinued 42 days after initiating treatment.

Case 2 (3-year-old female bulldog; 20.3 kg) was referred to us because of a history of chronic intermittent vomiting for the 2 years prior to her presentation. Recently, vomiting had been observed to occur 1 hour after meals, and frequency of nausea had increased. The patient was given commercial dry food and table food.

Physical examinations, CBC, serum biochemical analysis, radiography, and abdominal ultrasound showed no remarkable findings. The c-PLI ELISA result was negative.

The patient did not respond to pantoprazol (Pantosid, MyungMoon Pharma, Korea; 0.5 mg/kg, PO, q 12 h), domperidone (Domperidone, Kunwha Pharma, Korea; 3 mg, PO, q 12 h), and mosapride (Gasmotin, Daewoong Pharma, Korea; 0.75 mg/kg, PO, q 12 h), which were prescribed to prevent vomiting until a histopathological diagnosis was made.

Thus, we performed a gastrointestinal endoscopic examination to evaluate the cause of vomiting. In endoscopic examination, reflux esophagitis was found. Mild generalized gastric mucosal hyperemia (Fig 2) and foamy white fluid were also observed (Fig 2B). Gross endoscopic findings of the duodenum were not significant. Endoscopic biopsy samples were obtained from gastric mucosa.

Based on findings on the histopathological examinations, the patient was diagnosed to AG concurrent with *Helicobacter* infection. The gastric glands were found to be generally atrophic (Fig 3C) and were substantially colonized by *Helicobacter* organisms adjacent to the gastric epithelial cells. The hyperemia and mild inflammatory cells had infiltrated into the lamina propria (Fig 3D). After the diagnosis was determined, we decided to change the prescription, which

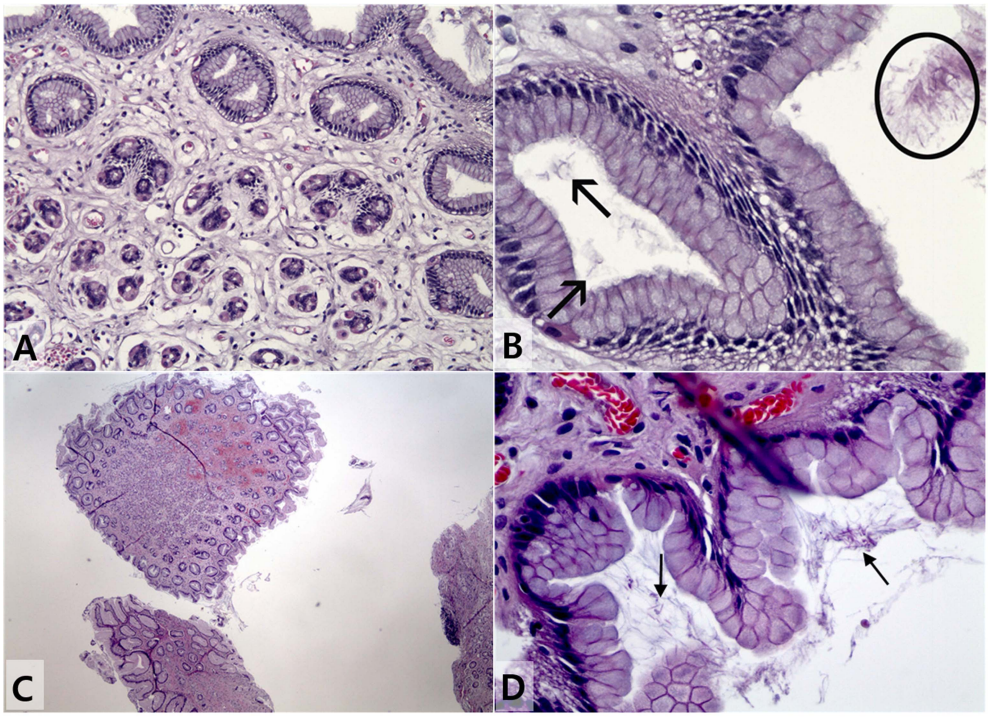

Fig 3. Results from histopathological examination of gastroscopic biopsy samples from case 1 (A and B) and case 2 (C and D). (A) Photomicrograph shows glandular atrophy and shallow gastric pits (× 60). (B) *Helicobacter spp.* was detected in the mucosal layer (circle) and lumen (arrows) of the gastric gland (× 600). (C) Gastric gland shows generalized atrophy (× 20). (D) *Helicobacter spp.* (arrows) are found in the lumen of the gastric pit with hyperemia and mild inflammatory cell infiltrates in the lamina propria (× 600).

included pantoprazol (Pantosid, MyungMoon Pharma, Korea; 0.5 mg/kg, PO, q 12 h), amoxicillin-clavulanic acid (Clavamox, Aurobindo Pharma Limited, India; 12.5 mg/kg, PO, q 12 h), and metronidazole (Flasinyl, CJ Cheiljedang Parma, Korea; 15 mg/kg, PO, q 12 h). After antibiotic therapy, the clinical signs dramatically improved and the patient was stabilized. All medications were discontinued 72 days after initial treatment.

Discussion

In human medicine, AG is a distinct feature of the parietal cell atrophy and neuroendocrine cell hyperplasia that might precede the development of anaplastic and neuroendocrine gastric adenocarcinomas (7). The host inflammatory response might contribute to the development of atrophy and could enhance inflammation, gastric atrophy, hypochlorhydria, and gastric cancer (6,10). *Helicobacter*-associated disease is considered a possibility when the histologic examination reveals inflammation with the presence of a significant number of *Helicobacter* organisms. Inflammation can occur in varying degrees (9) and infection seems to be related to an increase in gastric mucosal leukocytes, fibrosis, and lymphoid follicles (7). The lymphofollicular gastric infiltration is especially found in conjunction with the colonization of the gastric mucosa by *Helicobacter* (3). On the basis of the results of the experiments with gnotobiotic dogs, which are devoid of gastric bacteria, these dogs were verified to have no gastritis (3). These results are acceptable as the gastric lymphoid infiltrations represent an immune response to the bacterial antigens in the gastric mucosa (3).

According to previous reports (2,10,11), 67% to 100% of healthy dogs and 74% to 90% of vomiting dogs have gastric *Helicobacter spp.* infection. In veterinary medicine, as most dogs are asymptomatic, the cause and effect have not been clearly established between *Helicobacter spp.* infection and symptomatic gastric disease (12).

Biopsy with endoscopic findings can help in detecting *Helicobacter spp.*; furthermore, assessment of concurrent GI disease associated with *Helicobacter spp.* can be assessed. (7). Various endoscopic findings are seen in patients with gastritis, ranging from normal with mild gastritis to marked diffuse redness, mucosal swelling and friability with severe gastritis (4). Endoscopic findings of the present patients were almost normal with findings of only mild gastritis. Gross changes might be frequently minimal in dogs thought to have *Helicobacter* induced gastritis (9). We diagnosed the AG concurrent with *Helicobacter* infections through results of endoscopic and histological evaluations, which are one of effective diagnostic methods (12).

Most of the AG recovered after the removal of the cause (5). Preliminary studies report that up to 26% of affected dogs have a clinical response towards eradicating *Helicobacter* concurrent with AG (11). Therefore, we based our treatment plan for the *Helicobacter* infection in the present two cases on the results of these studies with the expectation that antibiotic therapy would be useful in the management of AG. In case 1, prednisolone was prescribed as an anti-inflammatory drug to manage the hematochezia associated with the enteritis. Several previous reports (6,8,10) demonstrated that antibiotic trials with a combination of metronidazole, amoxicillin, and famotidine showed improvement in clinical signs in 90%

of the 63 dogs and cats with *Helicobacter* infection. Moreover, in 70% of the animals that demonstrated resolution of gastritis, *Helicobacter spp.* was not detected in subsequent gastric biopsies (6,8,10). The present two cases responded well to amoxicillin-clavulanic acid with metronidazole. Gastric mucosal erythema was seen by endoscopic examination of case 2 and those findings suggested the possibility of progression to an ulcerative lesion if the infection had persisted. Thus, we prescribed pantoprazole for this case. According to a previous study (8), synergistic effects with a combination of antibiotics and a proton-pump inhibitor (PPI) can be expected. H_2-antagonists such as ranitidine or famotidine, and PPIs, such as omeprazole and pantoprazole, can enhance the antibacterial activity of metronidazole (8). Pantoprazole also works as an antimicrobial by inhibiting urease, an enzyme produced by *Helicobacter* (2,7).

Generally, *Helicobacter* associated gastritis in dogs have a good response to medical treatments with a good prognosis (12). In case 1, combination therapy with antibiotics and an anti-inflammatory dose of prednisolone worked well immediately. After the administration, clinical signs, such as vomiting and bloody diarrhea, improved and eventually resolved in case 1. Case 2 was treated with antibiotics and a PPI, and clinical signs improved dramatically.

Previous studies (6,10) suggest that a high reinfection rate (1% to 2% per year after treatment of *H. pylori*) could be the result of antibiotic resistance in non-*H. pylori Helicobacters* (NHPH) or the relatively high numbers of intracellular *Helicobacter* in dogs. *H. bizzozeronii* (65.2%), *H. heilmannii* (39.1%), and *H. felis* (8.7%) were identified as the predominant bacteria in infected dogs (11). According to a previous study, they can hide from metronidazole (10). The ability of NHPH to adhere to canine gastric mucosa occurs through a different adhesion mechanism mediated by proteins with alternative receptor specificity (1). It may be attributed to differences in the virulence of the infecting *Helicobacter spp.* or in the host immune response. Thus, much remains unknown about the effect of *Helicobacter* in canine AG and guidelines are needed regarding the treatment of AG concurrent with *Helicobacter spp.* infection in dogs.

This case report describes clinical, endoscopic, and histopathological findings of AG concurrent with *Helicobacter* infection.

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